CARCINOMA OESOPHAGUS A RE-EVALUATION OF RISK FACTORS, CLINICAL FEATURES & MANAGEMENT

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OF

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CERTIFICATE

This is to certify that this dissertation entitled "Carcinoma oesophagus- A re-evaluation of risk factors, clinical features & management" submitted by Dr.S.Chitra, to the faculty of Medical Gastroenterology, The Tamilnadu Dr.MGR Medical University, Guindy, Chennai-600032, in partial fulfillment of the requirement for the award of DM., Degree Branch IV (Gastroenterology) is a bonafide work carried out by her under my direct supervision and guidance.

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INTRODUCTION

Oesophageal cancer is a common malignancy with a very poor prognosis. It is the sixth most common fatal cancer in the world, causing over 300,000 deaths each year[1]. The five year relative survival rate in U.S.A was 14%, among the lowest for all cancer[2]. The main reason for this poor prognosis is that most cases are asymptomatic and go undetected until they have spread beyond the esophagus and are unresectable.

Using a age standarised rate, incidence is estimated worldwide at 11.5/100,000 in men and 4.7/100,000 in women. Much higher rates occur in certain regions of Asia, such as Cixian in China and of Africa[3]. While in most part of the world, the incidence is approximately 5/100,000 population, it may exceed 100/100,000 in countries like India & other Asian countries[4].

Among the digestive tract cancers in India, esophagus is the commonest site in both men and women.[5] It is the third leading cause of death in men and fourth leading cause in women. Lowest incidence has been reported from Punjab.[6]

At initial presentation, 50-60% of patients have a non resectable tumour. Surgical resection has long been considered to be the only curative treatment in the absence of distant metastasis or local lymph node metastases. However even after an optimal resection, which is feasible only in approximately

10% of cases, the overall survival rate ranges between 20% and 50% according to stage[7].

The importance of diet and nutrition in the etiology of many cancers has gained wide acceptance. Nutritional factors directly or indirectly has also been implicated in cancer oesophagus. In high incidence areas like Iran, where people neither smoke nor drink, lack of fresh fruits and vegetables, deficiency of vitamin A, riboflavin has resulted in mucosal damage[8]. Limited data are available from our country regarding risk factors analysis and presentation of cancer oesophagus. Hence the present study was undertaken to study about the risk factors, presentations, and treatment modalities of oesophageal cancer.

REVIEW OF LITERATURE

Cancer of the oesophagus remains a devastating disease because it is usually not detected until it has progressed to an advanced incurable stage. Worldwide, oesophageal cancer is the sixth leading cause of death from cancer. The lifetime risk of this cancer is 0.8% for men and 0.3% for women[9]. Modern imaging techniques, including contrast-enhanced computed tomography, magnetic resonance imaging, endoscopic ultrasonography, and positron-emission tomography are powerful tools in the detection, diagnosis, and staging of this malignancy. Early detection remains the elusive but essential goal of research. Only surgical resection at a very early stage has been shown to improve survival rates in patients with this disease.

Cancer of the oesophagus accounts for 7% of the gastrointestinal tract cancers in the United States. In the past, squamous cell carcinoma accounted for more than 95% of cases of oesophageal cancer. However, by the early 1990s, adenocarcinoma had become the most common cancerous cell type among white Americans, accounting for approximately one half of oesophageal malignancies in the United States and Europe. Squamous cell cancers still predominate among African American patients.

Worldwide, certain geographic regions have a high incidence of oesophageal squamous cell carcinoma. There exists a very high incidence area called

" oesophageal cancer belt" stretching from the region of the Caspian Sea eastward through Central Asia to northern China[10].

The incidence is 7.4/100,000 in UK, 87/100,000 in Japan and 100/100,000 in Asian countries[11.] In India the lowest incidence has been reported from Chandigarh 3.5/1,00,000 and highest from Dibugarh 19.7/1,00,000.Extremely high incidence rates, reaching endemic proportions have been reported from Jammu & Kashmir which seems to fall in the Asian oesophageal cancer belt. The unique personal and dietary habits and environmental factors in Kashmir have been attributed to the high risk[4].According to Chennai cancer registry, cancer esophagus ranks the third common malignancy in males and fourth common malignancy in females[12].

ANATOMY

The oesophagus is a muscular tube extending from the pharynx to the stomach. Histologically, the oesophageal wall contains 4 major layers:

- Mucosa or a mucous membrane composed of the lining epithelium; the lamina

propria, a layer of loose connective tissue enriched with capillaries and lymphatics; and the muscularis mucosae, a thin double layer of smooth muscle

- Submucosa, a loose connective tissue layer also rich in capillaries and lymphatics
- Muscularis externa (propria), consisting of 2 layers of muscle, the inner layer deployed circumferentially, and the outer layer arranged longitudinally
- Loose adventitia (unlike other areas of the gastrointestinal tract, which have a true serosa)

Because the oesophagus lacks a serosal covering, oesophageal carcinoma encounters few anatomic barriers to local invasion.

The cervical oesophagus is that portion extending from the inferior aspect of the cricoid cartilage to the thoracic inlet. Caudal to the thoracic inlet, the thoracic oesophagus is divided into thirds: The upper third extends from the thoracic inlet to the carina, and the middle and lower thirds are defined as the cranial and caudal halves of the remaining oesophagus from the carina to the gastroesophageal junction.

The oesophagus is drained by a rich network of lymphatics; therefore, precisely determining the particular draining lymph node chain for a given segment is often difficult. Jump lymph-node metastases occur when a node close to the involved oesophageal segment is not diseased, but a more distant node is diseased. For the

cervical oesophagus, cervical and supraclavicular lymph nodes are considered local, and mediastinal and upper abdominal lymph nodes are considered distant. For the upper and mid thoracic oesophagus, mediastinal lymph nodes are considered local, and involved cervical, supraclavicular, and abdominal lymph nodes are considered distant. For the lower oesophagus, mediastinal and perigastric lymph nodes are considered local, whereas involved cervical, supraclavicular, and celiac lymph nodes are considered distant.

PATHOPHYSIOLOGY

The most common types of oesophageal carcinoma are squamous cell carcinoma and adenocarcinoma.

SQUAMOUS CELL CARCINOMA

The normal oesophagus is lined by stratified squamous nonkeratinizing epithelium. Alcohol and tobacco use are the principal modifiable risk factors for oesophageal squamous cell carcinoma. According to the American Cancer Society, the combination of long-term alcohol ingestion and tobacco use is the most substantial risk factor. Nitrosamines and other nitrosyl compounds are found in pickled vegetables, smoked meat, and the water supply of certain geographic regions where the incidence of oesophageal squamous cell carcinoma is high. In regions in which the soil is deficient in

molybdenum and zinc, plants are impaired in their ability to metabolize nitrites to ammonia. This impairment permits potentially toxic nitrogen compounds to accumulate within plants that enter the human food supply.

Anecdotal associations have been made between oesophageal squamous cell carcinoma and chronic consumption of hot liquids, betel nuts, asbestos, air pollution, and diets high in spice content. Conversely, consumption of a diet high in fruits and vegetables has a protective effect.

Certain medical conditions predispose patients to the development of oesophageal squamous cell carcinoma. These include achalasia, lye strictures, head and neck tumors, celiac disease, Plummer-Vinson syndrome, tylosis, and prior exposure to radiation. Squamous cell carcinoma may arise in the setting of achalasia, typically after a period of 20 or more years, and it is believed to result from long-standing irritation by retained material. Of patients with strictures caused by lye ingestion, 3% develop squamous cell carcinomas after 20-40 years. The association of head and neck tumors with squamous cell carcinoma of the oesophagus is explained best by the common risk factors of alcohol and tobacco use.

Plummer-Vinson syndrome consists of dysphagia, iron-deficiency anemia, and oesophageal webs. Patients with this syndrome have an increased incidence

of postcricoid squamous cell carcinoma. Squamous cell carcinoma of the oesophagus occurs in almost all patients with tylosis, a rare autosomal dominant disorder characterized by esophageal papillomas and hyperkeratosis of the palms and soles.

Infection with human papillomavirus, particularly subtypes 16 and 18, has been implicated in the pathogenesis of oesophageal squamous cell carcinoma.

ADENOCARCINOMA

Adenocarcinoma, which is most common in the mid and distal oesophagus, arises from abnormal oesophageal mucosa in a well-characterized sequence. In reaction to chronic gastroesophageal reflux, metaplasia of the normal stratified squamous epithelium of the distal oesophagus occurs, resulting in a specialized intestinal glandular epithelium containing goblet cells called Barrett epithelium. Further genetic alterations in this epithelium lead to dysplasia, which may progress from low-grade to high-grade dysplasia and, ultimately, to adenocarcinoma.

Gastroesophageal reflux disease (GERD) is the most important factor in the development of Barrett epithelium. Of patients with GERD, 10% develop Barrett epithelium. Of patients with Barrett epithelium, 1% develop oesophageal adenocarcinoma, a risk that is 30-40 times higher than in the population without Barrett epithelium.

Smoking has been identified as a risk factor. Scleroderma and other motor disorders of the oesophagus that predispose patients to GERD increase the risk accordingly. Obesity, certain medications, environmental exposures, diet and nutritional habits have been implicated as additional risk factors.

RACE

African Americans are 3 times more likely than whites to develop cancer of the oesophagus. Although squamous cell carcinoma is relatively more common in African Americans, adenocarcinoma is more common in white Americans.

SEX

Males are 3 times more likely to develop oesophageal carcinoma than females.

AGE

Incidence of both squamous cell carcinoma and adenocarcinoma increases with age.

PROGNOSIS

Only early surgical resection improves survival rates in patients with this disease. Of patients with oesophageal cancer, 50% present with metastatic disease and most patients with apparent local disease develop metastases despite potentially curative local therapy. The primary cause of death in patients who are treated surgically is local recurrence, compared to other gastrointestinal tract tumors in which metastatic disease is usually the cause.

Prognosis depends on depth of tumor penetration through the oesophageal wall and the presence of lymph node metastases. The TNM system is used to classify the extent of disease.

Metastatic disease from a primary lesion in the lower oesophagus is classified as M1a if celiac nodes are involved. M1b designates metastatic disease beyond locoregional and celiac lymph nodes. For a primary lesion in the mid oesophagus, the M1a status is not applicable; metastatic disease beyond locoregional lymph nodes is designated M1b. For a primary lesion in the upper oesophagus, involvement of cervical lymph nodes is designated M1a; metastatic disease beyond locoregional and cervical lymph nodes is designated M1b.

Staging groups are formed on the basis of the TNM classifications and are used to guide therapy and predict the prognosis and survival.

Staging of Oesophageal Carcinoma

Stage	TNM	5-Year Survival Rate
0	Tis, NO, MO	75%
I	T1, NO, MO	50%
IIA	T2, NO, MO or T3, NO, MO	40%
IIB	T1, N1, MO or T2, N1, MO	20%
III	T3, N1, MO or T4, any N, MO	15%
IVA	Any T, any N, M1a	<1%
IVB	Any T, any N, M1b	<1%

CLINICAL FEATURES

SCC occurs predominantly in the middle and upper thirds of the oesophagus, while AdenoCA occurs predominantly in the distal third of the oesophagus and at the EG junction. Dysphagia is the most common symptom (90%), followed by odynophagia (50%). The presence of odynophagia coincides with an ulcerated tumor. Up to 75% of patients have experienced anorexia and weight loss when they seek medical attention. Chest pain or pain radiating to the back is a particularly sinister symptom, in that it implies invasion into neuromediastinal structures.

Advanced lesions typically appear exophytic as polypoid, fungating, or ulcerated masses. Lesions may be eccentric or circumferential. SCC of the oesophagus is an aggressively invasive tumor. Vocal cord paralysis accompanies recurrent laryngeal nerve invasion. Cough or recurrent pneumonia may indicate chronic aspiration as a result of oesophageal obstruction or oesophagorespiratory fistula due to direct tumor extension. Oesophagorespiratory fistulas occur in 5% of patients. The development of an oesophagorespiratory fistula confers a particularly poor prognosis with a median survival time of 1.5 to 4 months. Pulmonary, hepatic, bone, and brain metastasis may all be observed at presentation or during tumor progression. Hematemesis may be due to tumor ulceration. Exsanguinating bleeds occur with the development of an aortoesophageal fistula.

AdenoCAs are not similarly locally invasive. Lymphangitic and hematogenous metastases, however, do occur early to regional and distant lymph nodes and to the liver. Tumors limited to the mucosa have lymph node metastases in only approximately 3% of cases. However, once the tumor has penetrated the muscularis mucosa and invaded the submucosa, lymph node metastases are documented in 30% of cases, and when into the muscularis propria, in 60% of cases.

SCREENING

Screening refers to the application of diagnostic testing in asymptomatic individuals to determine if they have a pathologic process or a precursor lesion. Surveillance refers to the application of diagnostic testing in individuals known to have had the defined pathology or its precursor lesion to determine if the lesion has progressed, regressed, or remained stable, or if it has been previously treated whether the initial lesion remains or if new lesions are present. Screening for oesophageal cancer may employ nonendoscopic and/or endoscopic technique. Surveillance generally uses endoscopy. Cytologic and molecular techniques are the two non-endoscopic techniques that have been used with high-risk groups.

In the balloon technique, a deflated balloon covered by a cloth net or rubber ribbing is swallowed into the stomach, inflated, and then withdrawn, collecting exfoliated cells and scraping the mucosal surface of the oesophagus. At the upper oesophageal sphincter, the balloon is deflated and removed. In the sponge technique, a polyurethane mesh is compressed inside a gelatin capsule and attached to a string or a thin plastic stylet. The capsule is swallowed into the stomach, where the gelatin dissolves, and the mesh expands. Then the mesh is pulled up the oesophagus by the string, collecting exfoliated and scraped mucosal cells. In both methods, the collected cells are processed and stained for cytology and read for cellular abnormalities.

Among 500,000 Chinese who were screened, this technique had 90% accuracy in detection of cancer. Among lesions detected, 70% to 80% were early lesions[13].

The use of molecular markers is the second noninvasive modality that has been used to screen for SCC and its precursor lesions. They can sometimes be detected in clinical samples such as blood or stool that can be collected noninvasively. Molecular changes in DNA (e.g., hypomethylation, loss of heterozygosity, and mutations) can be amplified by PCR.

When screening is performed endoscopically, visual inspection to identify pathology is the first step. If chromoendoscopy is to be used, it generally is performed before performing biopsies. In the absence of staining, dysplastic mucosa may appear normal, nodular, white, red, or as an erosion or plaque. Early SCC is usually seen as an erosion, a plaque, or a nodule.

Early detection of SCC or dysplastic squamous epithelium may be enhanced with vital staining. Diluted Lugol's solution delivered endoscopically through a spray catheter has been most widely used. Lugol's solution is rapidly taken up by normal squamous mucosa, in contrast with dysplastic or malignant squamous epithelium, which remains unstained . This technique may also be applied to detect the

extent of mucosal surface involvement when endoscopic therapy is being contemplated for macroscopically recognized lesions. Tissue sampling from the unstained areas confirms the presence and extent of mucosal involvement.

The utility of mucosal iodine staining to improve endoscopic visualization of dysplasia and SCC was evaluated in the high-risk population of Linxian, China[14].

Methylene blue dye staining has been demonstrated to be useful in the detection of specialized columnar epithelium, but its accuracy in detecting neoplastic changes has not been confirmed consistently[15].

INVESTIGATIONS:

Laboratory results may indicate hypoalbuminemia and anemia secondary to bleeding or chronic disease. Hypercalcemia due to bony metastases or circulating humoral factors such as parathyroid hormone related peptide in SCC has been reported in 15% to 30% of patients[16]. Hepatic enzymes including alkaline phosphatase and the international normalized ratio may be increased in the setting of hepatic metastases.

Posteroanterior and lateral chest radiography is indicated in patients with chronic cough and abnormal findings on auscultative examination of the chest to

demonstrate pulmonary metastases and/or infiltrates suggestive of aspiration pneumonitis or oesophagorespiratory fistula. Findings may also include lateral deviation of the mediastinal contents, widening of the mediastinum, and oesophageal air-fluid levels.

BARIUM SWALLOW

Barium oesophagraphy remains the study of choice for characterization of oesophageal strictures. Oesophageal carcinoma may demonstrate a variety of appearances on barium oesophagrams.

- Lesions may be annular and constricting; intraluminal, polypoid, or masslike; infiltrative; ulcerating; or varicoid. A mixed pattern is most common.
- A double-contrast technique should be used for optimal sensitivity.
- The length and location of the involved oesophageal segment and the functional impairment resulting from the lesion should be reported.
- There are ten segments in the oesophagus - Marcel Brombert Classification.

Contrast radiographic studies should be used to confirm or refute suspected osophagorespiratory fistula and complete obstruction. In this context, barium is generally the preferred contrast agent, as opposed to diatrizoate meglumine, which may cause pulmonary inflammation or edema if it enters the airway via aspiration or a

fistula.

ENDOSCOPY

Flexible endoscopy is indicated in suspected oesophageal carcinoma. Endoscopy allows direct visualization of the oesophagus, as well as tissue sampling, to confirm the diagnosis. Endoscopy allows accurate characterization of the tumor's configuration, length, and localization. Endoscopy also allows initial relief of dysphagia in that dilation can be performed at the time of diagnosis. Standard endoscopic forceps biopsy typically yields a diagnosis. Biopsy procedures should be directed at non-necrotic areas. At least six biopsy samples should be obtained to yield an accuracy approaching 100%[17.] Occasionally submucosal spreading tumors require endoscopic ultrasound (EUS)–guided fine-needle aspiration for histologic diagnosis when standard forceps biopsies fail.

CT SCAN

Contrast-enhanced CT plays an important role in the staging of oesophageal carcinoma. Attention is directed in determining the extent of the local tumor; invasion of mediastinal structures; involvement of supraclavicular, mediastinal, or upper abdominal lymph nodes; and distant metastases. CT examination should extend from the thoracic inlet through the liver. Routine oral contrast material should be

administered. This may be positive contrast agent, such as dilute barium, or a negative intraluminal contrast medium, such as water. Techniques for virtual oesophageal endoscopy have also been described using effervescent granules and glucagon.

Key findings include the following:

- Eccentric or circumferential wall thickening is greater than 5 mm.
- Peri-oesophageal soft tissue and fat stranding may be demonstrated.
- A dilated fluid- and debris-filled oesophageal lumen is proximal to an obstructing lesion.
- Tracheobronchial invasion appears as displacement of the airway (usually the trachea or left mainstem bronchus) as a result of mass effect by the oesophageal tumor.
- Aortic invasion may be assessed in 2 ways.
    - The Picus method considers the arc of contact between the tumor and aorta (Picus, 1983). Loss of the periaortic fat plane over less than 45° suggests no aortic invasion, whereas contact over 90° or more is predictive of invasion of the aortic wall. Contact between 45-90° is indeterminate. Accuracy with this method is 80%.
    - Obliteration of the triangular fat space between the aorta, oesophagus, and spine is another predictor of aortic invasion.

A short-axis diameter exceeding 1 cm is considered abnormal for lymph nodes in all mediastinal locations except those in the subcarinal region, in which 1.4 cm is the upper limit of normal.

In a review of 838 patients with M1 disease, Quint et al found that metastases were diagnosed most commonly in the abdominal lymph nodes (45%); liver (35%); lung (20%); cervical and/or supraclavicular lymph nodes (18%); bone (9%); adrenal glands (5%); peritoneum (2%); brain (2%); or stomach, pancreas, pleura, skin or body wall, pericardium, or spleen (1% each).

Its sensitivity for the detection of lymph node metastases is in the range of 60-80%. Its specificity is higher, approximately 90%. Lesions in solid organs identified at CT may represent primary benign or malignant processes or metastatic disease, and biopsy is frequently necessary to obtain histologic proof.

MRI

MRI presents the advantage of direct multiplanar imaging capabilities, which may be of particular use in assessing tracheobronchial, aortic, and pericardial invasion. Currently, MRI has not yielded other significant advantages compared with CT in the staging of esophageal carcinoma.

Recent research studies suggest that T2-weighted MRIs obtained with an endoluminal coil can reveal 7 layers of the oesophageal wall. In the future, such resolution may offer superior assessment of the depth of tumor invasion. Preliminary studies have shown that the sensitivity and specificity of MRI for the determination of tumor invasion are equivalent to those of CT.

ENDOULTRASOUND

Unlike CT, EUS allows visualization of the distinct 5 layers within the oesophageal wall. Alternating circumferential layers define the mucosal interface (hyperechoic), the mucosa (hypoechoic), the submucosa (hyperechoic), the muscularis propria (hypoechoic), and the adventitial interface (hyperechoic). Such resolution permits the distinction of T1, T2, T3, and T4 tumors. Oesophageal carcinoma appears as a hypoechoic lesion disrupting the normal circumferential layers.

Local lymph nodes are also demonstrated by using EUS. Nodes are considered malignant if they are round, if they are hypoechoic, and if they have well-defined borders. Usually, benign nodes are hyperechoic and less well defined.

T-stage accuracy with EUS is in the range of 79-94%. Accuracy is better for T3 or T4 lesions than for T1 or T2 lesions[18]. Massari et al showed that a 12-

MHz transducer outperforms a 7.5-MHz transducer, with accuracy for T staging of 94% and 82%, respectively. N-stage accuracy is in the range of 69-90%; according to Rasanen et al, the technique probably outperforms CT and PET in the detection of locoregional lymph node metastasis.

EUS-guided fine-needle aspiration has significantly improved the ability to confirm malignant adenopathy. The procedure has been demonstrated to be safe and effective for puncturing periesophageal mediastinal nodes, as well as celiac lymph nodes[19]. The sensitivity, specificity, positive predictive value, and negative predictive value for EUS combined with FNA in the assessment of celiac nodes range from 53% to 98%, 77% to 100%, 79% to 100%, and 82% to 100%, respectively[20].

NUCLEAR MEDICINE

PET is quickly becoming a standard oncologic imaging modality. The technique is useful not only for the primary detection of tumor and metastases but also for the further characterization of abnormalities discovered by using other imaging modalities.

2-[Fluorine 18]-fluoro-2-deoxy-D-glucose (FDG) is the most commonly used radiopharmaceutical. Radiopharmaceuticals other than FDG can be used in PET imaging. Carbon-11 choline has received particular attention. Choline, a

component of the cell membrane, is taken up by actively dividing cells.[11]C-choline PET scanning has been shown to outperform FDG PET scanning in the detection of malignant mediastinal lymph nodes. With this agent, tumor containing mediastinal lymph nodes as small as 4 mm have been identified.The short half-life of [11]C-choline (approximately 20 min) will likely limit its use to major academic centers. The sensitivity of FDG PET in assessing nodal metastasis is reportedly 33-83%, but studies have shown the superiority of FDG PET to CT and EUS for determining the N status[21]. FDG PET is more sensitive than CT for the detection of distant metastases.

TREATMENT

Oesophageal cancer is a treatable disease that is rarely curable. The overall 5-year survival rate in the subgroup of patients amenable to surgery ranges from 5% to 20%.

Primary treatment modalities include surgery alone or chemotherapy with radiation therapy. Combined modality therapy (chemotherapy plus surgery, or chemotherapy and radiation therapy plus surgery) is under clinical evaluation. Endoscopic mucosal resection[22] and/or photodynamic therapy[23] in selected patients with superficial carcinoma is also under clinical evaluation. Effective palliation may be obtained in individual cases with various combinations of surgery, chemotherapy, radiation therapy, and endoscopic therapy.

PRIMARY THERAPY

Surgery is the treatment of choice for early (superficial) tumors. Once symptoms (dysphagia, in most cases) are present, oesophageal cancers have usually invaded the muscularis propria or beyond and may have metastasized to lymph nodes or other organs.

Surgical treatment of resectable oesophageal cancers is associated with a 3% to 10% operative mortality rate[24]. Operative morbidity includes anastomotic leaks and strictures (20%) and cardiopulmonary complications. One approach advocates transhiatal oesophagectomy with anastomosis of the stomach to the cervical esophagus. A second approach advocates abdominal mobilization of the stomach and transthoracic excision of the oesophagus with anastomosis of the stomach to the upper thoracic oesophagus or the cervical oesophagus. Although a transthoracic resection permits better visualization of the tumor and a more thorough dissection of adjacent lymphatics, the thoracotomy increases the risk of cardiopulmonary complications, and if the transhiatal technique is used, places the patient at risk for an anastomotic leak in the chest. The result of one study suggests that the transhiatal approach has a lower rate of perioperative (mainly pulmonary) complications[25].

As an alternative to surgery, definitive radiation therapy in combination with chemotherapy has been studied. One series, evaluating radiation therapy and

chemotherapy with fluorouracil and mitomycin, produced a 75% local control rate, associated with improved swallowing, and a 30% actuarial disease-free survival rate (18% overall survival) at 5 years for stage I and stage II patients[26]. An Eastern Cooperative Oncology Group trial of 135 patients showed similar results, in that chemotherapy plus radiation yielded a better 2-year survival rate than radiation therapy alone[27].

The logic of neoadjuvant chemoradiation is appealing. It offers potential early treatment for micrometastatic disease and it could assist surgical resection by downstaging cancer. Additionally, patients seem to tolerate preoperative chemoradiation better than postoperative therapy[28].

ENDOSCOPIC THERAPY FOR SUPERFICIAL CARCINOMA

Early oesophageal cancers are defined as those confined to the mucosa or submucosa, T1N0M0 . In Japan there has been a further division of T1 lesions. $T1_M$ implies mucosal involvement, and submucosal invasion may be termed $T1_{SM}1$ (upper third); $T1_{SM}2$ (middle third); and $T1_{SM}3$ (lower third). Submucosal invasion ($T1_{SM}$ 1-3) carries a 5% to 40% risk of lymph node metastasis[29].

Superficial oesophageal cancers have been treated endoscopically by mucosal resection (EMR), laser therapy, or argon plasma coagulation. Photodynamic therapy (PDT) also uses endoscopy. Superficial tumors have also been treated with

radiation therapy and brachytherapy. The most common technique employs a transparent suction cup, fitted to one end of the endoscope[30]. This technique, like most others, uses preresection submucosal injection to create a pseudopolyp, which is then resected by snare polypectomy. The band ligation method is a variation on this technique. Lift and cut methods generally employ a two-channel endoscope[31]. Recently, insulated tipped electrocautery knives have been used to perform resection without the need for suction [32].

Five-year cure rates for intramucosal squamous cell carcinomas have been as high as 100%, while those that penetrated the submucosa had 5-year survival rates of 54% to 59%.Complication rates of 7% were reported in large series and were primarily hemorrhage, perforation, and stenosis [33].

Early oesophageal adenocarcinoma and HGD have been treated endoscopically in the setting of Barrett's oesophagus. Endoscopic mucosal resection has been used alone or in combination with photodynamic therapy or with thermal therapies. When the expertise is present and if the pathology can be localized, endoscopic resection is increasingly becoming the treatment of choice.

PALLIATIVE THERAPY

Most patients with oesophageal cancer have advanced disease at the time of initial presentation and less than 20% survive 1 year after the time of diagnosis.

At diagnosis, approximately 50% of patients with oesophageal cancer have metastatic disease and are candidates for palliative therapy.

Standard palliative treatment options may include radiation therapy, chemotherapy, combination chemoradiotherapy, intraluminal brachy-therapy and endoscopic therapies. All of the preceding modalities may be offered in combination with endoscopic tumor dilation, intubation, or ablation. Chemotherapy has yielded partial responses among patients with metastatic distal oesophageal AdenoCA. Many chemotherapeutic agents are active in oesophageal cancer. Objective response rates of 30% to 50% are commonly reported with platinum-based combination regimens with fluorouracil, a taxane, or a topoisomerase inhibitor [34].

The main goal of endoscopic therapy is palliation of dysphagia, which contributes to improved nutritional status and quality of life. Endoscopic palliative therapies can be divided into those methods that displace tissue (dilation, stenting) and those that ablate tissue. Ablative therapies destroy tissue by using contact thermal, noncontact thermal, cytotoxic injection, and photodynamic therapies. Bleeding and oesophagorespiratory fistulas are other complications that can be managed with endoscopic therapy, but symptoms of pain and anorexia cannot be managed endoscopically. Oesophagorespiratory fistulas, which are a dire complication of SCCA

of the oesophagus, as well as primary pulmonary malignancies that invade the oesophagus, are particularly well managed with oesophageal stent placement.

DILATION

Dilation achieves tumor displacement by the use of lateral shearing forces to stretch and tear the stenotic tissue. Dilation may be performed as primary palliative therapy or adjunctively to assist longer-lasting thermal or stent therapy.

There are two types of commonly used dilators: polyvinyl dilators (Savary-Guilliard or American type) and hydrostatic through-the-scope (TTS) balloons. Advantages of dilation include simplicity, low cost, wide availability, short procedure time, and relative safety. Most patients derive initial benefit from dilation therapy to a luminal diameter that allows passage of a liquid to soft diet (12 mm). However, dilation can be complicated by perforation in up to 10% of cases. The main disadvantage of dilation therapy is that its relief is often short-lived, and as the disease progresses, symptom-free intervals decrease in duration, requiring more frequent sessions.

CONTACT THERMAL THERAPY

Contact thermal ablation therapies are no longer widely used for palliation of dysphagia associated with advanced oesophageal cancer. The electrosurgical tumor probe (BICAP tumor probe) is a contact thermal ablation technique used primarily in the palliation of circumferential oesophageal malignancies. The assembled apparatus has a central lumen that enables the system to be passed over a guidewire. The tumor probe

produces a predictable depth of injury because contact with nondesiccated tissue is required to complete the circuit.

The procedure is performed under combined endoscopic and fluoroscopic guidance. In the recommended retrograde approach, the tumor probe is passed over a guidewire and through the area of luminal narrowing. Under fluoroscopic guidance, the probe is then pulled back in retrograde fashion so that the electrosurgical component of the tumor probe is in contact with the malignant tissue. The active electrode is 1.5 cm in length, so by withdrawing the tumor probe at 1-cm intervals, a small amount of overlap is achieved and uniform tissue injury is delivered to the treatment zone. At follow-up endoscopy 48 hours postprocedure, necrotic debris is removed and additional therapy applied on the basis of clinical results.Technical success with increased luminal diameter and significant improvement in dysphagia has been consistently reported for 80% to 90% of patients[35]. Generally, one or two treatment sessions achieved a mean duration of palliation of 7 to 8 weeks.

ENDOSCOPIC LASER THERAPY

Endoscopic laser therapy is a noncontact means of thermal ablation. Laser photoablation has been used extensively in the palliation of malignant dysphagia associated with oesophageal cancers.

Neodymium:yttrium-aluminum-garnet(Nd:YAG), potassium titanyl phosphate (KTP), and argon lasers have been used for thermal therapy of GI

malignancies. Laser therapy has the capacity to vaporize tissue in addition to producing coagulation necrosis. When feasible, the retrograde method is preferred. For annular lesions, circumferential treatment should be applied at each level. ELT, in addition to tumor ablation and coagulation necrosis, often produces some tissue edema and swelling, which may result in transient luminal narrowing. When complete luminal obstruction is present, ELT in antegrade fashion is necessary.

Once the desired extent of luminal patency has been attained, follow-up endoscopy should be carried out in 3 to 4 weeks to assess the need for repeat ELT versus expectant therapy for worsening dysphagia. A contrast barium swallow may be considered after completion of ELT to document the effects of therapy. The diet should include liquid nutritional supplements.

ELT achieves technical success with luminal patency in 97% of cases, whereas functional success defined by relief of dysphagia occurs in 70% to 85%. Sixty to seventy percent of patients remain free of dysphagia for 3 to 6 weeks. Only 20% to 25% of patients treated remain symptom free for 3 months or more [36]. Complications occurred in 4.1% of cases in a survey of 1359 cases. Perforation occurred in only 2%; the procedure-related mortality rate was 1%; the incidence of fistula or hemorrhage was 1%; and sepsis occurred in 0.5% to 1%. Perforations are more likely to occur in patients who have had prior radiation therapy.

Favorable and unfavorable characteristics of endoscopic laser therapy have been identified. Characteristics that favor successful ELT include a mucosal, exophytic, or polypoid endoscopic appearance of the tumor. Straight segments are more easily treated and have better outcomes than angulated segments. Short tumor segments, less than 6 cm, are more effectively treated than more extensive ones. Lesions that occur in close proximity to the upper esophageal sphincter are difficult to treat because aiming the laser beam is more difficult in this location. Likewise, lesions at the EG junction that are horizontal in orientation are more difficult to treat because of difficulty in aiming.

ARGON PLASMA COAGULATION

Argon plasma coagulation is emerging as an alternative to laser photocoagulation for ablation of superficial luminal digestive tract lesions. Because of the limited depth of injury achieved by APC (2 mm), there is limited benefit in treating advanced bulky tumors.

CYTOTOXIC INJECTION THERAPY

Cytotoxic injection therapy is theoretically attractive in that it is cheap, simple, and readily available. A variety of chemical agents have been used for palliation of oesophageal cancers, both by debulking tumors and by controlling bleeding [37]. Injectates have included chemotherapeutic agents and chemical sclerosants such as polidocanol, ethanol, and sodium morrhuate. Tissue destruction is brought about by chemical necrolysis. Disadvantages are the inability to control the depth of tissue injury

and the lack of immediately visible tissue effects.

PHOTODYNAMIC THERAPY

The biological effects of photodynamic therapy (PDT) are photochemical, as cytotoxicity is induced by nonthermal laser light energy. A photosensitizing agent is administered intravenously and is selectively retained in tumor cells. The photosensitizing agent is then activated by low-dose, wavelength-specific laser light delivered in close proximity to the lesion. Activation by light produces a local cytotoxic effect mediated by singlet oxygen. Two randomized comparative trials reported palliation equivalent to that of Nd:YAG laser therapy. PDT for palliation of malignant dysphagia has been reported using aminolevulinic acid, an exogenous porphyrin precursor, as a photosensitizing agent and nonlaser (high-power xenon lamp) light source with encouraging results in a phase II trial. A major advantage of PDT is that large areas may be treated during a single session. Complications and adverse events associated with PDT include skin photosensitivity, chest pain, atrial fibrillation, odynophagia, and stricture formation.

OESOPHAGEAL STENTS

Expandable metallic oesophageal stents are indicated for the palliation of luminal stenosis due to oesophageal cancer and for the management of oesophagorespiratory fistulas. Self-expanding metallic stents have replaced their

semirigid plastic predecessors because they are easier to place, achieve more effective palliation, and are associated with fewer complications. Covered or coated SEMSs are the most effective means of palliating oesophagorespiratory fistula .

Accurate tumor length measurement is critical to successful SEMS deployment. Prior radiographic contrast swallowing studies may be helpful to characterize a tortuous stenosis or an oesophagorespiratory fistula. The type, length, and diameter of stent selected are individualized to the specific patient's condition and the operator's experience. Dilation is necessary, however, when luminal obstruction does not permit the endoscope to pass.

Accurate tumor margin marking is critical to effective stent placement. One or more marking techniques may be used. Externally affixed radiopaque markers become less useful when the patient moves during delivery device insertion. Simply marking the proximal and distal tumor margins, as measured endoscopically, on the delivery device is sufficient in many cases. More precise marking of the tumor margins or center point can be achieved by submucosal injection of a radiocontrast agent using a sclerotherapy needle or by endoscopic placement of metallic mucosal clips. Familiarity with the specific stent delivery apparatus, the significance of its radiopaque markings, and the degree of anticipated foreshortening is critical.

Postprocedure, patients who have stents placed across the EG junction should have instructions for head-of-bed elevation greater than 30 degrees at all times. Antiemetics and antitussives may be used when retching, coughing, or hiccupping is significant early on to prevent stent dislodgment. Clear liquids may be initiated on the same or following day and the diet advanced as tolerated. Dietary recommendations should be individualized. Patients are advised to chew food well; avoid stringy meats, fruits, and vegetables; flush the oesophagus frequently with liquids during meals.

A variety of oesophageal SEMSs are commercially available. They are covered and uncovered stents.The Wallstent II (Microvasive, Boston Scientific) consists of a bilayer chromium alloy tubular mesh coated with a polyurethane sleeve between two mesh tubes. The Flamingo Wallstent is a popular modification of this covered stent with an exaggerated proximal flange to reduce occurrences of distal stent migration.

The Ultraflex stent (Microvasive, Boston Scientific) consists of a knitted nitinol wire tube. The stent is constrained on the introducer catheter by a spiral retention suture. Unraveling the suture deploys the stent. One unique advantage of this stent is that models with distal or proximal release systems can be selected.

The “Z”-stent (Cook Medical) is made of stainless steel wires shaped in a Z configuration. It has uncovered segments in the proximal and distal sections that have reduced this risk. A model designed with a latex “wind-sock” extending from the distal opening of the stent (Dua stent) and intended to prevent gastroesophageal reflux has been marketed for EG junction and distal oesophageal cancers for which the stent must bridge the EG junction.

The Polyflex (Boston Scientific) is a completely coated self-expanding nonmetallic (plastic) stent recently introduced and approved by the Food and Drug Administration for palliation of malignant and benign dysphagia. Published series have shown the Polyflex stent to be safe and effective in relieving malignant dysphagia[38]. Published series have reported uniformly good results for palliation of dysphagia, as well as oesophagorespiratory fistulae.

Covered SEMSs were effective in palliating fistulas in 70% to 100% of cases. For this complication of oesophageal cancer, SEMSs are uniquely qualified. Potential complications of SEMS placement include tumor ingrowth or tumor overgrowth (5% to 20%), stent migration (10%), and chest pain. Laser or contact thermal therapy is effective for ablation of tumor overgrowth of previously placed stents. Other complications may include procedure-related perforation, food bolus impaction, bleeding, foreign body sensation, and reflux oesophagitis. Gastrorespiratory

aspiration is of particular concern among patients in whom the stent crosses the EG junction.

ENTERAL NUTRITION

Most patients with advanced oesophageal cancer have compromised nutritional status. When feasible, enteral is preferred to parenteral nutrition support. Enteral nutrition support may be indicated in an attempt to improve functional status before and after surgery, during chemoradiotherapy, and as an adjunct to other palliative measures.

Enteral access can be achieved surgically, radiographically, or endoscopically. A surgical jejunostomy should routinely be created at the time of esophageal resection. Percutaneous endoscopic gastrostomy (PEG) is safe and effective for nonoperative candidates. PEG placement is not appropriate for candidates for subsequent oesophagectomy with gastric pull-up. Direct gastric feeding may be contraindicated in patients with SEMSs that extend beyond the EG junction and in postesophagectomy patients because of its increased risk of gastrorespiratory reflux and aspiration. Poor gastric emptying is observed in many patients who have EG junction carcinomas that extend into the gastric cardia and fundus. In these patients, endoscopic enteral access can be achieved by creating a direct percutaneous endoscopic jejunostomy or a PEG with a jejunal feeding tube extension[39].

ANALGESIC THERAPY

Pain due to tumor ulceration and neural invasion is observed in patients with advanced oesophageal cancer. Pain may be significant in some patients after stent insertion, as a result of radial expansion. This pain generally lasts for 1 to 2 weeks. Oesophageal cancer pain should be managed with narcotic analgesia. Long-acting sustained release preparations may be supplemented with shorter-acting agents. Parenteral applications such as transdermal patches have obvious appeal for use in patients with dysphagia.

PRIMARY PREVENTION

According to the World Cancer Research Fund, 50% to 70% of SCC could be avoided by implementation of guidelines for a healthy lifestyle. There is some evidence that anti-inflammatory medication may prevent deterioration to cancer in intestinal metaplasia.

SECONDARY PREVENTION

It is aimed at detecting neoplasia at a curable stage in asymptomatic persons. High resolution endoscopy is useful in identifying early lesions. In western countries, endoscopic screening is recommended in persons with high consumption of alcohol and tobacco. Screening is justified after treatment for head and neck cancer. Factors justifying surveillance are male sex, a prolonged symptomatic history of GERD, continuous smoking and presence of peptic stricture or ulcer in intestinal metaplasia cases.

AIM OF THE STUDY

1. To study about the demographic features of carcinoma oesophagus.

2. To assess the influence of risk factors in the causation of carcinoma oesophagus.

3. To study the clinical features of carcinoma oesophagus and to correlate the level of hold up of food with the site of lesion.

4. To assess the incidence of operability of tumour at the time of presentation.

5. To study about the various modalities of treatment available for these patients and to assess the symptomatic improvement after treatment.

MATERIALS AND METHODS

Patients included in the study were recruited from the department of digestive health and diseases, Government Peripheral hospital, Anna Nagar, Chennai. The study period was from September 2005 to March 2008.

Consequetive patients diagnosed to have carcinoma oesophagus formed the study group. Healthy individuals who were accompanying the patients formed the control group.The control group individuals were matched with patients for age (± 5 years) and sex.

A detailed proforma was completed for both the patients and controls. A detailed history about dietary habits and social habits such as smoking, alcohol, tobacco chewing were recorded. Clinical history about dysphagia, site of hold up, anorexia and weight loss was obtained and thourough clinical examination was done. Body mass index was calculated for all.

Investigations included haemoglobin, erythrocyte sedimentation rate, barium swallow, U G I Scopy & biopsy and CTSCAN of the chest & upper abdomen were done. In those cases where scope cannot be negotiated beyond the growth, dilatation was done and extent detected. Histopathological grading was done by the pathologist. Treatment was individualized according to the stage of the disease at presentation. Follow up of the patients was done.

The statistical analysis was done using EPI INFO 6. Odds ratio

estimates of relative risk was calculated for the risk factors. Univariate and multivariate analysis were done. P value of < 0.05 was found to be significant. Percentage calculation was done whenever appropriate.

RESULTS

The total number of cases and controls were 155 each. The male female ratio was 1.67: 1.

The incidence of cancer oesophagus was 7.1% in patients below the age of 40 years. It slowly increased and reached the maximum in 5th decade and then slowly declining. The incidence was 12.9% in patients above the age of 70.

Most of them were from places in & around Chennai (66.4%). Similar distribution was seen in controls also. Most of them did some manual work on daily wage basis. About 80% of the female patients were housewives.

	CASES*(n=155)*	***CONTROLS****(n=155)*
SEX		
Male	*97(62.6%)*	*97(62.6%)*
Female	*58(37.4%)*	*58(37.4%)*
AGE *(mean) Years*	*58.3*	*58.3*
AGE DISTRIBUTION		
< 30	*2 (1.3%)*	*2(1.3%)*
31-40	*9 (5.8%)*	*7(4.5%)*
41-50	*31(20%)*	*25(16.9%)*
51-60	*55(35.5%)*	*52(33.5%)*
61-70	*38 (24.5%)*	*42(27.1%)*
> 70	*20(12.9%)*	*27(17.4%)*
RESIDENCE		
Chennai	*87 (56.1%)*	*83(53.6%)*
Coimbatore	*1(0.7%)*	*3(1.9%)*
Salem & Erode	*27(17.4%)*	*23(14.8%)*
Arakkonam & Cuddalore	*6(3.9%)*	*14(9%)*
Kanchipuram & Chengalpet	*16(10.3%)*	*12(7.7%)*

Others	*18(11.6%)*	*22(14.2%)*
OCCUPATION		
Farmer	*23(14.8%)*	*46(29.7%)*
Housewife	*49(31.6%)*	*52(33.5%)*
Dependant & Retired	*31(20%)*	*10(6.5%)*
Electricians	*2(1.3%)*	*4(2.6%)*
Others	*50(32.3%)*	*43(27.7%)*
LITERACY		
Illiterate	*76(49.0%)*	*59(38.1%)*
Literate	*79(51%)*	*96(61.9%)*
RELIGION		
Hindu	*138(89%)*	*142(91.6%)*
Christian	*7(4.5%)*	*13(8.4%)*
Muslim	*10(6.5%)*	*0*

About 49% of patients were illerate whereas only 38% of controls were illerate. Majority of the patients and controls belonged to hindu religion (89% and 92%). There were no muslims in control group but 6.5% of the patients belong to muslims.

RISK FACTORS

No one in the control & case group had history of corrosive intake or achalasia cardia. One patient in case group and 3 in control group had history of gastric surgery. 4 patients had past history of head & neck malignancy and radiotherapy. None in the control group had malignancy or radiotherapy. 7 patients had postcricoid web prior to or during the diagnosis of cancer oesophagus.

	CASE	***CONTROL***	***ODDS RATIO***	***95% CI***	***P VALUE***
Corrosive					
Yes	*0*	*0*			
No	*0*	*0*			
Achalasia					

Yes	*0*	*0*			
No	*0*	*0*			
Gas Surgery					
Yes	*1(0.7%)*	*3(1.9%)*			
No	*154(99.4%)*	*152(98.1%)*			
Radiation					
Yes	*4(2.6%)*	*0*			
No	*151(97.4%)*	*0*			
Head & Neck Ca.					
Yes	*4(2.6%)*	*0*			
No	*151(97.4%)*	*0*			
P V Synd					
Yes	*7(4.5%)*	*0*			
No	*148(95.5%)*	*0*			
Alcohol					
Yes	*67(43.2%)*	*30(19.4%)*	*1.7*	*0.65-4.49*	*0.28*
No	*88(56.8%)*	*125(80.7%)*			
Smoking					
Yes	*79(51%0*	*27(17.4%)*	*1.16*	*0.43-3.11*	*0.77*
No	*76(49%0*	*128(82.6%)*			
Tobacco					
Yes	*100(64.5%)*	*38(24.5%)*	*4.63*	*2.46-8.71*	0.00
No	*55(35.5%)*	*117(75.5%)*			
Family h/o Cancer					
Yes	*9(5.8%)*	*3(1.9%)*	*4.14*	*0.81-21.22*	*0.09*
No	*146(94.2%)*	*152(98.1%)*			
Tea / Coffee > 2 cups/day					
Yes	*123(79.4%)*	*33(21.3%)*	*11.53*	*6.24-21.32*	*0.00*
No	*32(20.7%)*	*122(78.7%)*			
Veg/ Fruits daily					
Yes	*33(21.3%)*	*74(47.7%)*	*0.42*	*0.22-0.81*	0.01
No	*122(78.7%)*	*81(52.3%)*			

About 43% & 51% of cases used alcohol and smoking respectively, whereas only 19% & 17% used alcohol and smoking in the control group. On doing univariate analysis the risk of oesophageal cancer was found to be 1.7

times higher with alcohol consumption, 1.16 times higher with smoking, 4.63 times higher with tobacco, 4.14 times higher in patients with family history of cancer, 11.53 times higher with tea & coffee > 2 cups per day and 0.42 times less common in patients who took green vegetables & fruits daily.

On doing multivariate analysis, only tobacco consumption, tea & coffee intake> 2 cups/day & not taking vegetables and fruits daily were found to be important independent risk factors.

SYMPTOM ANALYSIS

SYMPTOMS	YES	NO
Dysphagia	*154(98.4%)*	*1(1.6%)*
Odynophagia	29(18.7%)	126(81.3%)
Heartburns	7(4.5%)	148(95.5%)
Regurgitation	63(40.6%)	92(59.4%)
Aspiration	67(43.2%)	88(56.8%)
Vomiting	65(41.9%)	90(58.1%)
GI Bleed	3(1.9%)	152(98.1%)
Reduced Appetite	39(25.2%)	116(74.8%)
Weight Loss	134(86.5%)	21(13.5%)

DYSPHAGIA SCORE	1	2	3	4
	10(6.5%)	24(15.5%)	100(64.5%)	20(12.9%)
DURATION(DAYS)	<15	15-30	30-90	>90
	18(11.6%)	43(27.7%)	62(40%)	31(20%)
SITE OF HOLD UP	THROAT	UPPER CHEST	MID CHEST	LOW CHEST
	90(58.1%)	22(14.2%)	36(23.2%)	7(4.5%)

Dysphagia was present in 98.4% of patients. Majority of the patients(64.5%) had grade 3 dysphagia according to Atkinson et al score. About 40% of patients had dysphagia for 30-90 days.11.6% had short duration (15 days)

of dysphagia. Site of hold up was in the throat in 58.1%& in midchest in 23.2% of patients. Odynophagia was seen in 18.7%, heartburns in 4.5%, regurgitation in 40.6% of cases.Aspiration in 43.2%, vomiting in 41.9% , GI bleed in 1.9% were recorded. 25.2% had reduced appetite and 86.5% had weight loss.

CLINICAL FINDINGS

The body mass index was between 16- 20 in 84.5% and it was < 15 in 4.5% where as only 11.1% had BMI in between 21-25. Pallor was present in 94.8% of patients. Only 12 cases had lymph node enlargement. None had either tylosis or acanthosis nigricans. 16 cases had aspiration pneumonitis. 10 cases had hepatomegaly with secondaries.CVS & CNS were normal in all cases.

B M I	**<15**	**16-20**	**21-25**
	7(4.5%)	131(84.5%)	17(11%)
PALLOR	**YES**	**NO**	
	147(94.8%)	8(5.2%)	
LYMPH NODE	12(7.7%)	143(92.3%)	
TYLOSIS	0	155(100%)	
ACANTHOSIS NIGRICANS	0	155(100%)	
	NORMAL	**ABNORMAL**	
RESPIRATORY SYSTEM	139(89.7%)	16(10.3%)	
CARDIO VASCULAR SYSTEM	155(100%)	0	
ABDOMEN	145(93.5%)	10(6.5%)	
CENTRAL NERVOUS SYSTEM	155(100%)	0	

INVESTIGATION

Haemoglobin was low in 86.5% of case and 96.1% had raised ESR. Barium study was done in 140 cases, of which 40% had irregular narrowing, 34.2% had irregular narrowing with shouldering. Tracheo-oesophageal fistula was seen in 6 cases. Typical rat tail appearance was seen in 10.3% of cases.

HAEMOGLOBIN	< 10 Gms	>10Gms						
	134(86.5%)	21(13.5%)						
ESR	<10mms	>10mms						
	6(3.9%)	149(96.1%)						
BARIUM SWALLOW	IRR NAR(1)	RAT TAIL(2)	SHOULD(3)	TOF(4)	NOT AVAIL(5)	1,4	1,3	2,4
	62(40%)	16(10.3%)	1(0.7%)	0	15(9.7%)	6(3.9%)	53(34.2%)	2(1.3%)
UGI SCOPY								
SITE	CER ESO(1)	UPP THO(2)	MID ESO(3)	LOW ESO(4)	1,2	2,3	3,4	2,3,4
	1(0.7%)	11(7.1%)	32(20.7%)	40(25.8%)	10(6.5%)	21(13.5%)	36(23.2%)	4(2.6%)
LENGTH	<2	3-5	6-8	>9				
	6(3.9%)	52(33.5%)	56(36.1%)	41(26.5%)				
TYPE	ULCER	PROLIF	U P	POLYP				
	35(22.6%)	65(41.9%)	49(31.6%)	6(3.9%)				
EXTENT	CIRCUM	ECCEN						
	123(79.4%)	32(20.7%)						
T O F	Yes	No						
	11(7.1%)	144(92.9%)						
HISTOLOGY								
S C C (90.3%)	WELL	MOD	POOR					
	22(15.7%)	90(58.1%)	28(18.1%)					
A D C (7.1%)	0	9(81.8%)	2(18.2%)					
OTHERS	4(2.6%)							
CT SCAN	NARROW	NAR, AOR	NAR, LUNG	NAR, LUN,LIV	NAR,AOR,LIV	NAR,LIV	NA,AO,LUN	
	43(27.7%)	97(62.6%)	1(.7%)	1(.7%)	3(1.9%)	7(4.5%)	3(1.9%)	

U G I Scopy was done for all cases. It showed lesion in cervical oesophagus in 0.7%, upper thoracic oesophagus in 7.1%, mid thoracic oesophagus in 20.7% and lower oesophagus in 25.8% of cases. Lesions involving 2 segments constituted 45.8%, among which 23.2% of cases had growth involving both mid & lower thoracic oesophagus. About 36.1% had growth of 6-8 cms in length, 26.5% had growth of more than 9 cms, where as only 3.9% had growth of < 2cms. 41.9% had proliferative type of growth, 22.6% and 31.6% had ulcerative and ulceroproliferative growth respectively.3.9% had polypoidal lesion. 79.4% had circumferential growth and 20.6% had eccentric lesion. Tracheo-oesophageal fistula was documented in 11 cases.

Histopathological examination showed squamous cell carcinoma in 90.3% , adenocarcinoma in 7.1% and other types in 2.6% of cases. CTScan showed narrowing alone in 27.7% and narrowing with aortic involvement in 62.6%. Approximately 36.8% were subjected to radiotherapy and surgery was done in 8 cases. 11 cases had SEMS stent deployed for palliation. Chemoradiotherapy was done for 25.8% of cases. 2 cases had nasogastric tube placement alone.

TREATMENT	**NUMBER OF PATIENTS**
SURGERY	8 (5.2%)
SEMS STENT	4 (2.6%)
CHEMOTHERAPY	4 (2.6%)
RADIOTHERAPY	57 (36.8%)
DILATATION / SURGERY	1 (0.7%)
DILATATION / RADIOTHERAPY	24 (15.5%)
RADIOCHEMOTHERAPY	40 (25.8%)
RADIOTHERAPY / STENTING	2 (1.3%)
CHEMOTHERAPY / OTHERS	2 (1.3%)
CHEMO/ STENT/DILATATION	1 (0.7%)
CHEMO/ DILATATION	6 (3.9%)
STENT/ DILATATION	4 (2.6%)
OTHERS	2 (1.3%)

Follow up was not available for 7 cases. 20 cases had lost follow up in between the study. Mean duration of follow up was 123.1 days(ranging from 15 to 965days).

FOLLOW UP	***AVAILABLE***		**N A**	
	148 (95.5%)		7 (4.5%)	
POST TRT DYS SCORE	**0**	**1**	**2**	**3**
	3 (2%)	117 (79%)	16 (10.8%)	12 (8.1%)
DURATION (MEAN IN DAYS)	156.4			
POST RT STRICTURE	**YES**		**NO**	
	19(15.4%)		104(84.5%)	
ANAST STRICTURE	**YES**		**NO**	
	3(33.3%)		6(66.6%)	

Post radiation stricture was seen in 15.4% of cases and 33.3% developed anastamotic stricture. On follow up, 2 patients had recurrence, one patient developed malignancy in stomach (SCC) and one developed tumour overgrowth with occlusion of stent. One patient developed non neoplastic nodular lesion in stomach.

DISCUSSION

The mean age of carcinoma oesophagus in this study was 58.3 years. Schlansky et al in his report stated that the age at initial presentation was 66 years which was similar to this present study[40]. The male female ratio in this study was 1.67:1,similar to that quoted by R.K. Tandon et al[41]. The mean age of occurrence for cancer oesophagus was 52 years and male female ratio was 1.5:1, according to Khuroo et al [2]. Parkin et al report a low prevalence of 7.6/100 000 of oesophageal cancer in the age group of 35-39, with an increasing incidence above the age of 45 [42]. A similar trend was seen in this study also.Tandon et al showed increased incidence in 4th and 5th decade in his study [41]. Male preponderance was noted all over the world with low sex ratio in India. This may be due to high prevalence of betal nut and tobacco quid chewing among the Indian females.

28% of the cases were illiterate and 32% received only primary school education according to Tandon et al [41]. But in this study, 49% & 38% were illiterate in cases and controls respectively. In the present study, oesophageal cancer was more common among the hindus, followed by muslims and then Christians.The Mumbai cancer registry had reported a preponderance among hindus & muslims with low incidence among Christians[43]. Khuroo et al in his study showed significant differences in hindus, muslims and sikh population. Sikhs had highest incidence in his study [2]. In this study, 47% involved in unskilled occupation and 31.6% were

housewives. But Tandon et al showed that only 21.4% were involved in unskilled occupation[41].

In western countries, a casual relationship has been established with the consumption of alcohol and tobacco. Tobacco was found to interact with light to moderate consumption of alcohol (0.1-30 gms/day) as a risk factor[44].According to Malken et al, 85% of oesophageal cancer was attributed to alcohol and tobacco use in U SA & Europe [6]. The influence of alcohol is probably related to quality of alcohol consumed rather than type or concentration. In Tandon et al study, the relative risk was 1.85 times higher with alcohol which was similar to this study. Smoking and tobacco chewing increased the risk by 1.16 and 4.63 times in this study, when compared to 2.38 and 2.36 times in Tandon et al study[41]. Case controlled studies carried in India revealed alcohol drinking to be positively attributed with oesophageal cancer[45]. Alcohol may contain carcinogenic chemicals and other contaminants that are known or suspected carcinogens. These include N-nitroso compounds, mycotoxin, urethane, tannins, inorganic arsenic and other pesticide residues and asbestoes filtration products that may influence the carcinogenic process[46].Nandakumar et al also showed increased risk(1.95) with smoking [47].

Sanghivi et al reported a relative risk of 1.5 – 3.5 for cancer oesophagus from betal quid chewing[48.] Smoking in association with betal quid chewing and alcohol consumption has a multiplicative risk. The combined use also appears to influence the site of cancer oesophagus[49].

Tandon et al reported a protective role of vegetables and fruits[7]. Similar results were observed from a study from Mumbai. Notani et al found a risk of 2.62 times with decreased vegetables intake [50]. In this study, the risk was 0.42 times lower in cases who took daily vegetables and fruits. The increased risk due to low consumption of green vegetables may be due to absence of anticarcinogenic agents like vitamin A, C, selenium, folic acid, dietary fibre and other plant sterols. These anticarcinogens bind to carcinogens in the lumen.

Khuroo et al had shown that salted tea consumption among Kashmiris was responsible for high incidence of cancer oesophagus[2]. This has been attributed to the high content of nitrosamines. The dietary pattern in India varies in different parts. Increased risk has been reported with smoked and fermented items. Thermal trauma when drinking hot beverages > 70^0 C may play a role in Asia and South America[44].In this study, taking tea & coffee >2 cups / day increased the risk by 11.53 times.

Family history of cancer increased the risk by 4.14 times in this study. Post cricoid web was seen in 7 cases and head and neck malignancy and radiation were seen in 4 cases each. All were directly related to development of cancer oesophagus. Only one case in the patient group had undergone gastric surgery whereas 3 had undergone surgery in control group. So this was not found to be significant.

Dysphagia was the predominant symptom (98.4%) in this study which was similar to the other studies. According to Schlansky et al, 55% of cases had

dysphagia, 38% had odynophagia and 15% had weight loss. Less commonly patients reported in descending order of frequency, emesis, GI bleed, mass abdomen, anaemia, cough, fatigue, anorexia & hoarseness[40]. According to Dr.Richard Schatzke in 1958 , involvement of about half the circumference is required to produce dysphagia [8]. Odynophagia was present in 18.7%, GI bleed in 1.9%,weight loss in 86.5%of the cases in this study. Most of the patients had grade 3 dysphagia and site of hold up was in the throat in 58.1% of cases whereas only 7.2% of cases had growth in cervical and upper thoracic oesophagus. 59% of cases had gradeII dysphagia according to Berquist et al[51.] 84.5% of the cases had BMI of between 16 to20 which indicated their poor nutritional status. Pallor was present in 94.8% of cases and 7.7% of cases had cervical lymph node enlargment. 6.5% had secondries liver at the time of presentation.

Haemoglobin was low in 86.5% and increased ESR was found in 90.1% of cases. Barium swallow revealed irregular narrowing alone in 40% of cases, narrowing with shouldering (corner sign) in 34.2% of cases and rat tail appearance in 10.3%. Wion and Felson described 3 types of roentgenographic configuration of cancer of oesophagus – infiltrative, polypoid, and ulcerative. The infiltrative form present with narrowing in concentric manner. Shouldering is called as corner sign. Lymphoma usually present as polypoidal lesion.

In this study, endoscopy showed growth in lower oesophagus in 25.8%, mid oesophagus in 20.7%, involving both middle and lower oesophagus in 23.2% & upper and mid thoracic oesophagus in 13.5%.Berquist et al showed growth in

distal oesophagus in 76%, mid oesophagus in 18% and proximal oesophagus in 5% similar to this study[51]. Cancer oesophagus occurred in upper third in 1.8%, middle third in 60.4% and lower third in 37.8%in Khuroo et al' s study, which was different from this study[2]. Schalansky et al showed 59% in mid oesophagus, 18% in lower thoracic oesophagus and 23% in upper oesophagus for squamous cell carcinoma and 97% in lower thoracic oesophagus and 3% in mid thoracic oesophagus for adenocarcinoma[40]. The length of the tumour was mostly ranged from 6-8cms in 36.1%of cases and > 9cms in 26.5%.

Earliest manifestation – hold up in neck can be misleading indication of focus of disease. Length is the most common characteristic in determining localized or advanced state. The most frequently published dimension of an early cancer is < 5cms length, if the length is < 5 cms, 50% develop nodal metastasis; if it is > 5 cms 90% develop nodal metastasis[8].Tracheo- oesophageal fistula was present in 7.1%. 79.4% had circumferential growth and only 20.7% had eccentric growth.

In this study, 90.3% had squamous cell carcinoma, 7.1% had adenocarcinoma and 2.6% had other varieties such as small cell and baso squamous cell carcinoma. R.Lambert and Hainaut reported that SCC is the most common type and ADC is relatively rare. In many countries in Europe and Asia, the proportion of ADC is < 10%; higher figures are only shown in the Caucasian population in USA, Australia and northen Europe[52]. Khuroo et al showed SCC in 85.3%, ADC in 14.6% of the cases and leiomyosarcoma in 2 cases[2].Small cell carcinoma of esophagus was reported by

Deshpande et al in 1996[53]. CTScan showed liver secondaries in 13.4%, lung secondaries in 3.3%. Aortic involvement was noted in 75.4% of cases which precluded surgery in these patients.Vyas et al reported 57% of cancer are localized, 14% had distant metastasis and another 14% had continuous extension[54].

Berquist et al's study showed stenting in 67% and brachytherapy in 25% of cases, since he studied patients with advanced disease [51].Combined chemoradiation improve the prognosis of patients suffering from advanced cancer oesophagus.The response rate was 64% with 25% complete response[55]. Van de schoot proposed that new paclitaxel based neoadjuvant chemotherapy followed by surgery in cases with stage 2 or 3 disease would be very useful[56]. The metaanalysis which analysed 1116 patients altogether concluded that compared with alone, neoadjuvant therapy improved 3 year survival and decreased local and regional recurrence. Homs et al studied 200 patients with SEMS placement for malignant dysphagia, 52 of whom had previously received chemotherapy(n=35), radiotherapy (n=8) or both(n=6). The dysphagia score improved in all patients from a median of 3 to 0 at 4 weeks[57]. In this study, only 8 patients underwent surgery, 11 underwent SEMS placement and sizable number of patients underwent radiotherapy alone or along with chemotherapy. According to Jeevan kumar et al, all the 69 patients who underwent stenting (choos stent) showed improvement in the dysphagia score[58].

Follow up showed improvement of dysphagia from 3 to 1 in 79% and 3 to 0 in 2%. Still 8% had grade 3 dysphagia – may be related to post radiation /

anastamotic stricture, recurrence or dysmotility. Post radiation stricture developed in 15.4% and anastamotic stricture in 33.3% of cases.

CONCLUSION

- *Oesophageal carcinoma is one of the commonest digestive tract cancer in Chennai.The etiopathogenisis seems to be multifactorial in origin.*
- *There are more number of female cases probably due to increased tobacco chewing and illiteracy.*
- *Smoking and alcohol intake increases the risk significantly and low intake of vegetables aud fruits also is detrimental.*
- *Dysphagia is present in almost all patients.*
- *There is no correlation between the site of lesion and site of hold up of food.*
- *Delayed presentation precluded curative surgical treatment in most of the cases.*
- *Many treatment modalities are available for these cases- surgery, radiotherapy(curative & palliative),chemotherapy, chemoradiotherapy and endotherapy. Multimodal treatment seems to offer good results.*
- *Symptomatic improvement occurs in 75% of cases.*
- *Reducing tobacco usage and dietary improvement are complimentary, inexpensive and a practical way to control cancer oesophagus in India.*

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PROFORMA

NAME: DDHD NO:

AGE: YRS IP NO:

SEX: MALE / FEMALE V OGD NO:

RESIDENT OF (> 5 YRS): ADDRESS:

OCCUPATION:

SYMPTOMS DURATION

DYSPHAGIA FOR DYSPHAGIA SCORE:

SOLIDS:

LIQUIDS:

BOTH:

ODYNOPHAGIA:

HEARTBURNS:

REGURTITATION:

ASPIRATION:

VOMITING:

GI BLEED:

SITE OF HOLD UP: (SPECIFY FROM MANUBRIUM STERNI IN CMS)

REDUCED APPETITE:

WEIGHT LOSS:

HISTORY OF CORROSIVE INTAKE:

ACHALASIA:

HISTORY OF GASTRIC SURGERY:

HISTORY OF RADIATION:

HISTORY OF HEAD & NECK MALIGNANCY:

P V SYNDROME:

CONTACT WITH CHEMICALS / FERTILISERS: YES / NO

ALCOHOL: BRAND :

QUANTITY : DURATION :

SMOKING: BRAND :

QUANTITY : DURATION :

TOBACCO :

CHEW: DURATION: FREQ / DAY

STUDIED UPTO :

FAMILY HISTORY OF CARCINOMA : (SPECIFY)

RELIGION : HINDU / MUSLIM / CHRISTIAN /OTHERS

DIET DETAILS:

VEG /FRUITS DAILY YES/ NO

DRINKS: NO. OF CUPS / DAY (200ML / CUP)

COFFEE :

TEA :

ON EXAMINATION :

HEIGHT : CMS WEIGHT : KGS BMI :

PALLOR :

LYMPH NODE : YES /NO

TYLOSIS : YES / NO

ACANTHOSIS NIGRICANS : YES / NO

RESPIRATORY SYSTEM : CLEAR / CREPS

CARDIO VASCULAR SYSTEM : NORMAL / ABNORMAL

ABDOMEN : MASS EPIGASTRIUM YES / NO

LIVER SIZE

SURFACE

BRUIT / RUB

CENTRAL NERVOUS SYSTEM :

METASTATIC SYMPTOM / SIGNS

INVESTIGATIONS :

HB %

ESR MMS

BARIUM SWALLOW:

IRREGULAR NARROWING

RAT TAIL APPEARANCE

SHOULDERING

TOF

UPPER GASTRO INTESTINAL ENDOSCOPY:

SITE OF GROWTH

LENGTH OF GROWTH

ULCERATIVE / PROLIFERATIVE / POLYPOIDAL

CIRCUMFERENTIAL / ECCENTRIC

TOF

HISTOLOGY:

SQUAMOUS CELL CARCINOMA

WELL DIFFERENTIATED

MODERATELY DIFFERENTIATED

POORLY DIFFERENTIATED

ADENO CARCINOMA

WELL DIFFERENTIATED

MODERATELY DIFFERENTIATED

POORLY DIFFERENTIATED

OTHERS

CT SCAN CHEST & UPPER ABDOMEN:

NARROWING

AORTA INFILTRATION

LUNG SECONDARIES

LIVER SECONDARIES

TREATMENT:

SURGERY: (IF OPERABLE)

IF INOPERABLE - -

RADIOTHERAPY

CHEMOTHERAPY

SELF EXPANDING METALLIC STENT

DILATATION

FOLLOW UP:

POST TREATMENT DYSPHAGIA SCORE:

FOLLOW UP PERIOD:

POST RT STRICTURE : YES / NO

ANASTOMOTIC STRICTURE : YES / NO